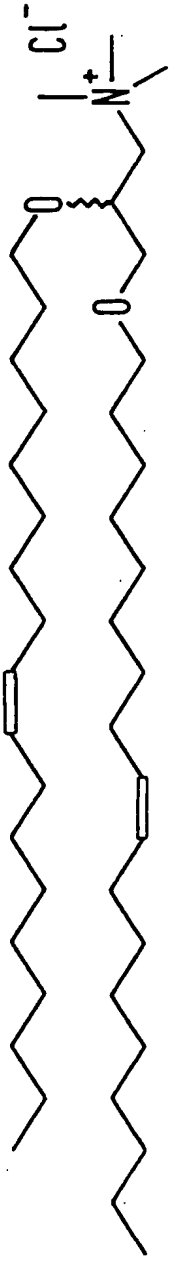
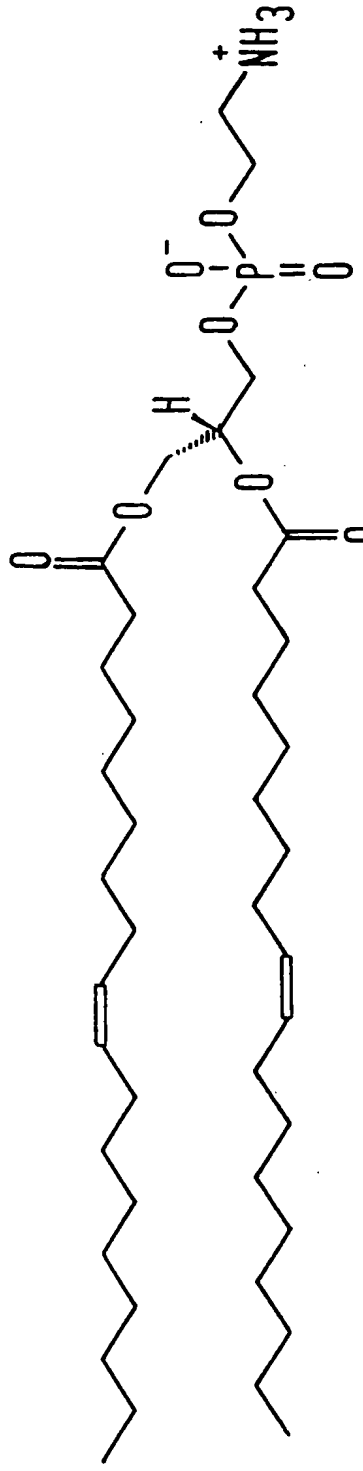


DOTMA *N*-[1-(2,3-dioleoyloxy)propyl]-*N,N,N*-trimethyl ammonium chloride

FIG. 1



DOPE Dioleoylphosphatidyl ethanolamine

FIG. 2

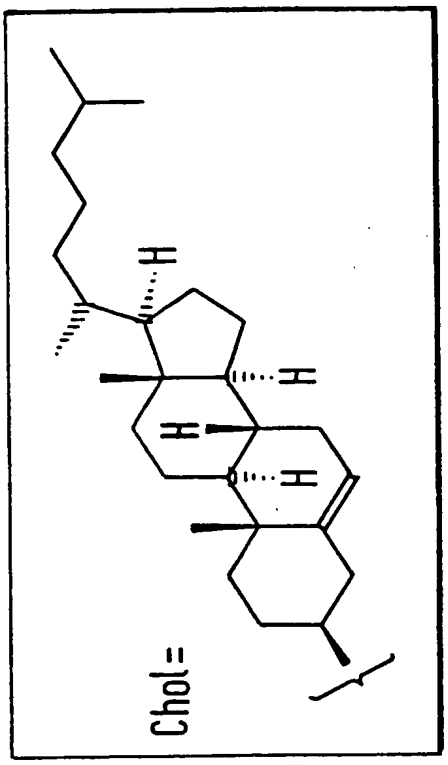
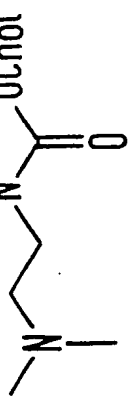
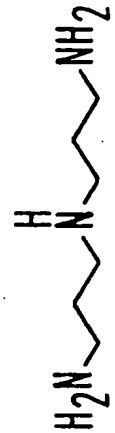


FIG. 3

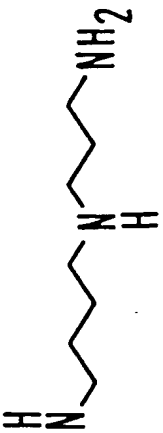


3β-[(*N*,*N*-dimethylaminoethyl)carbamoyl]cholesterol

DC-Chol

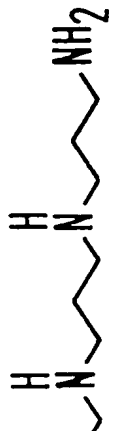


Norspermidine

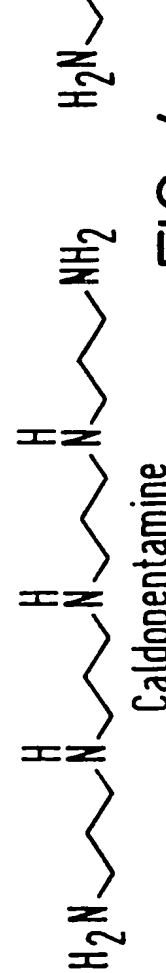


Spermine

Spermidine



Norspermine



Caldopentamine

FIG. 4

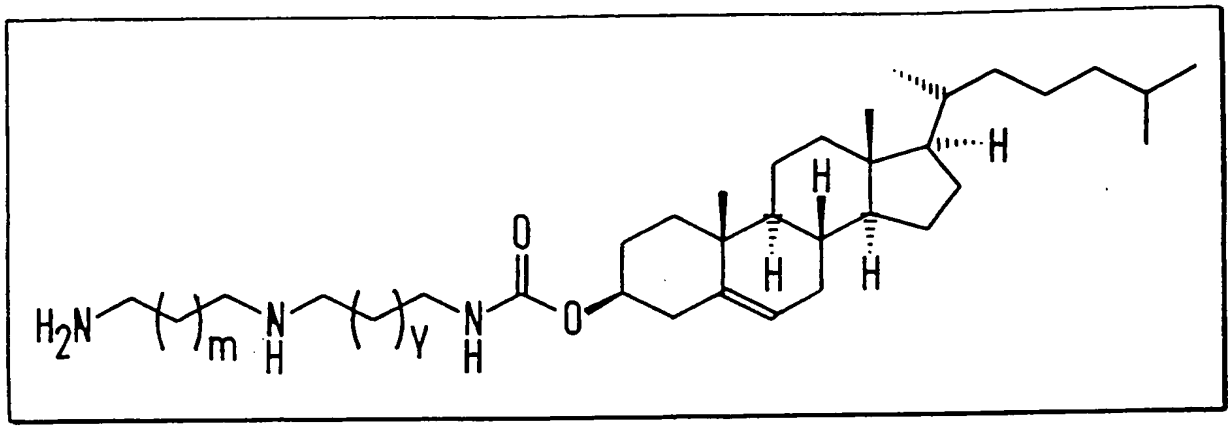
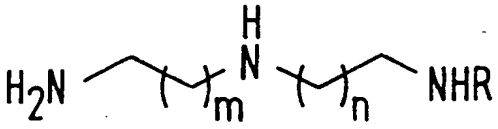
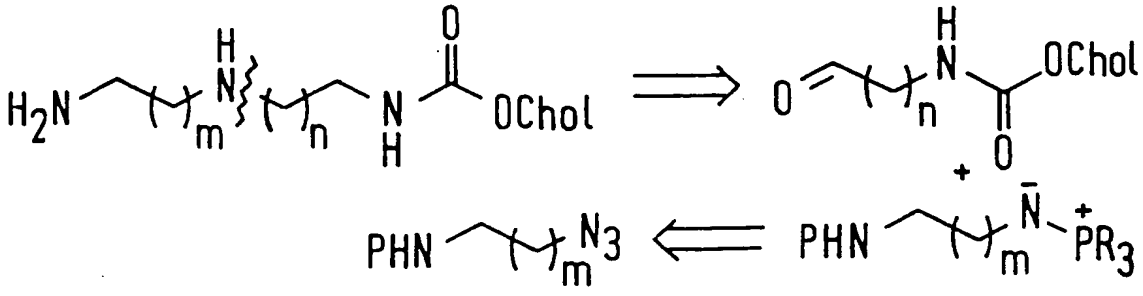


FIG. 5



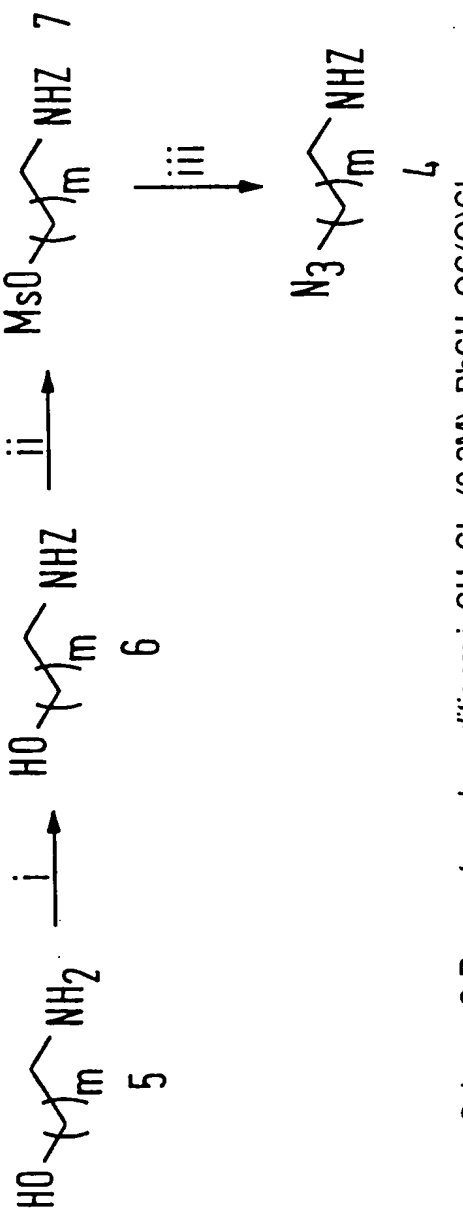
2, R = C(O) OChol
3, R = H

FIG. 6



Scheme 1

FIG. 7

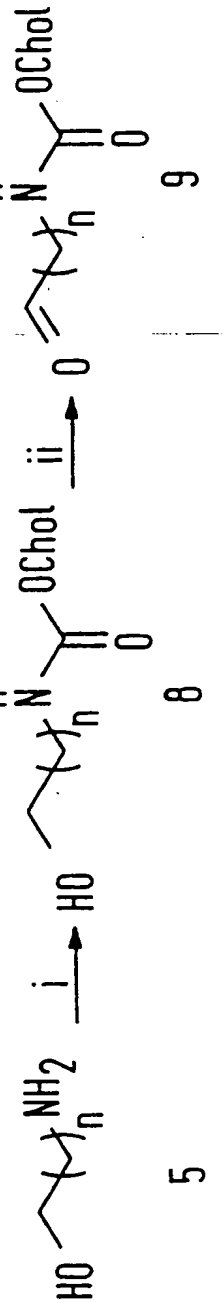


Scheme 2 Reagents and conditions: i, CH_2Cl_2 (0.2M), $PhCH_2OC(O)Cl$ (0.45 eqv), 10h; ii, CH_2Cl_2 (0.2M), Et_3N (3 eqv), CH_3SO_2Cl (2.5 eqv) 0°C to r.t., 15min; iii, DMF (0.15M), NaN_3 (5 eqv), NaI, 80°C, 2h

	6a	6b	6c	7a	7b	7c	4a	4b	4c		
m	1	2	3	1	2	3	1	2	3		
YIELD / %	89	86	92	97	88	95	98	90	96		

Table 1

FIG. 8

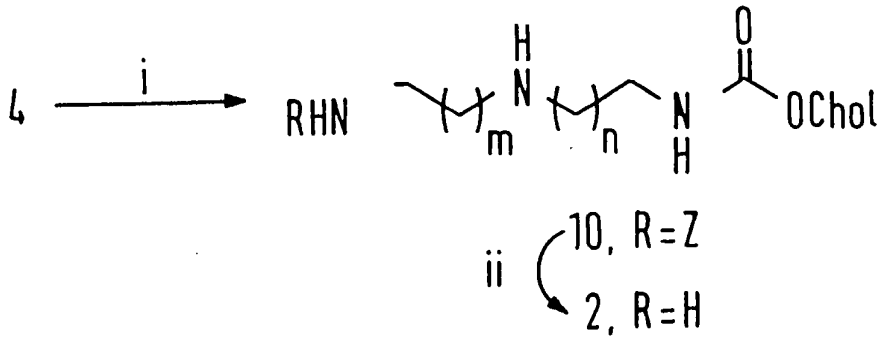


Scheme 3 *Reagents and conditions*: i, CH_2Cl_2 (0.2M), CholOC(O)Cl (0.45 eqv), 5h; ii, a, CH_2Cl_2 (0.1M) $(COCl)_2$ (1.5 eqv), DMSO (3 eqv), -78°C, 15min; b, 8, 15 min; c, *i*-Pr_2NEt (3 eqv) to r.t.

FIG. 9

	8a	8b	9a	9b	
n	1	2	1	2	
YIELD / %	98	99	97	93	

Table 2



Scheme 4 *Reagents and conditions*: i, a, THF (0.5M), 4 Å molecular sieves, PMe3 (1.15 eqv), 30 min; b, **9** (1.1 eqv), 3h; c, EtOH (0.5M), $NaBH_4$ (2 eqv), 20 h; ii, EtOH (0.2M), *c*-C_6H_{10} (20 eqv), 10% Pd(C) (0.5 eqv), reflux, 30 min

FIG. 10

	10a	10b	10c	10d	10e	10f	2a	2b	2c	2d	2e	2f
m	1	2	3	1	2	3	1	2	3	1	2	3
n	1	1	1	2	2	2	1	1	1	2	2	2
YIELD / %	79	72	89	83	87	90	99	99	99	99	99	99

Table 3

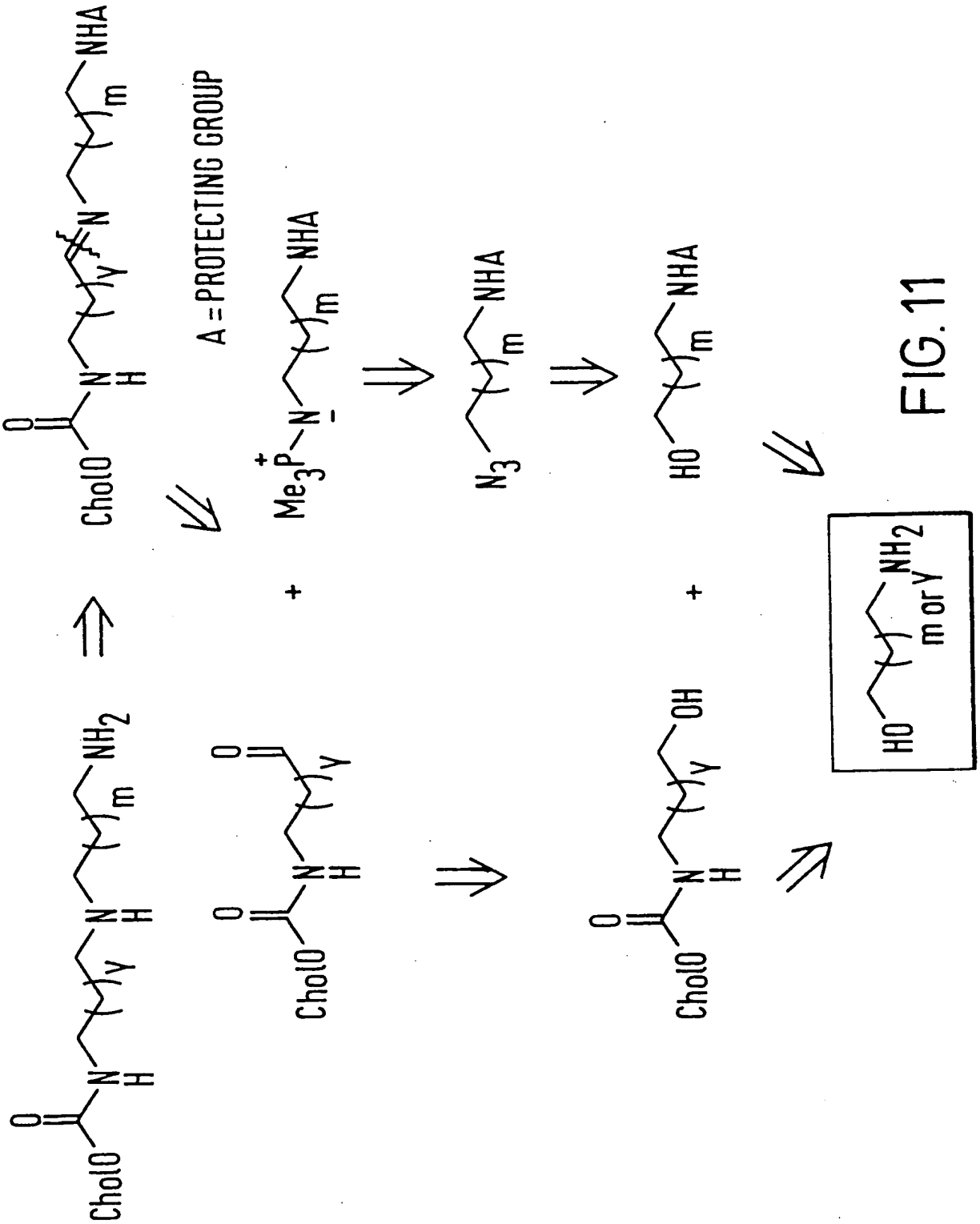


FIG. 11

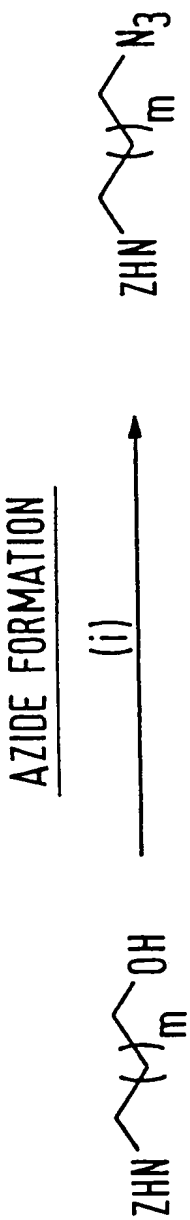


FIG. 12

m	yield (%)
0	87
1	92
2	90

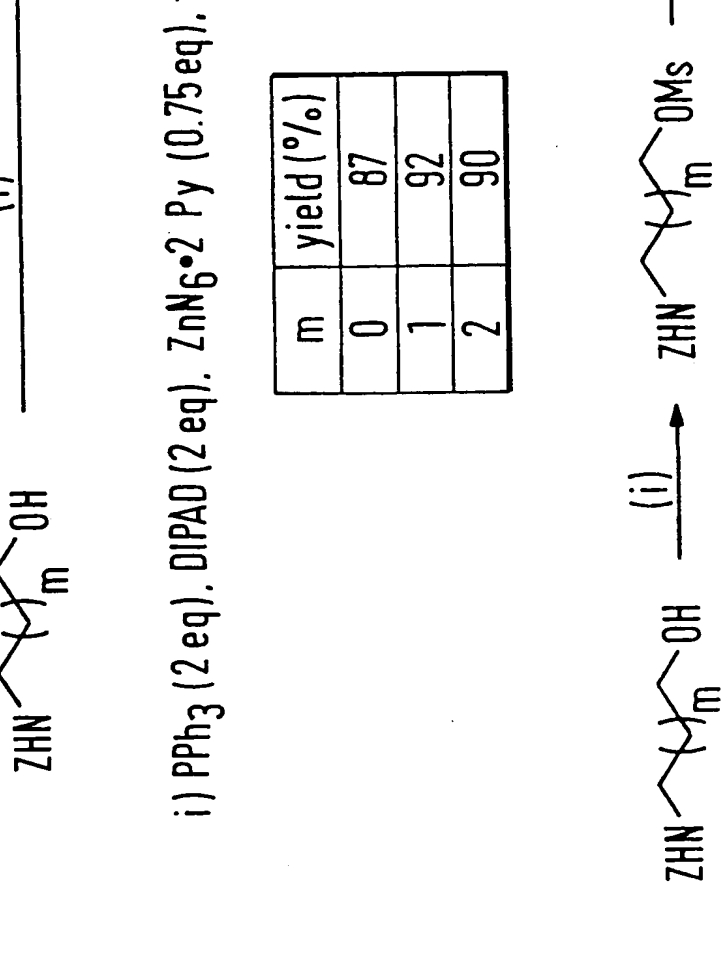


FIG. 13

m	Overall yield (%)
0	95
1	79
2	91

Y	yield (%)
0	97
1	93

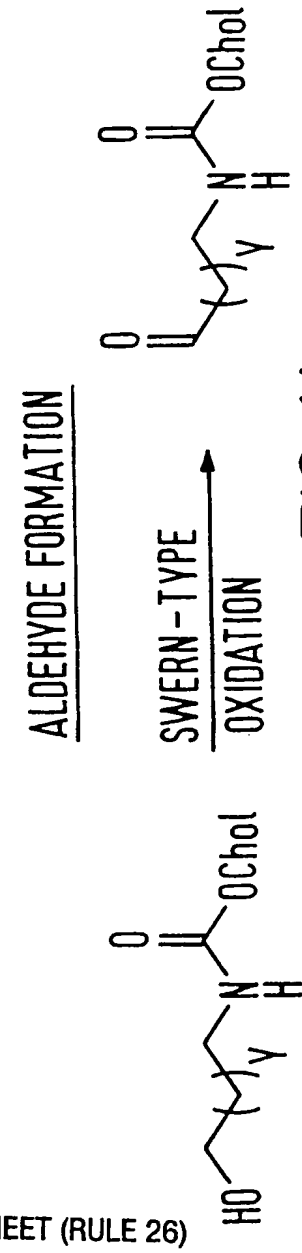
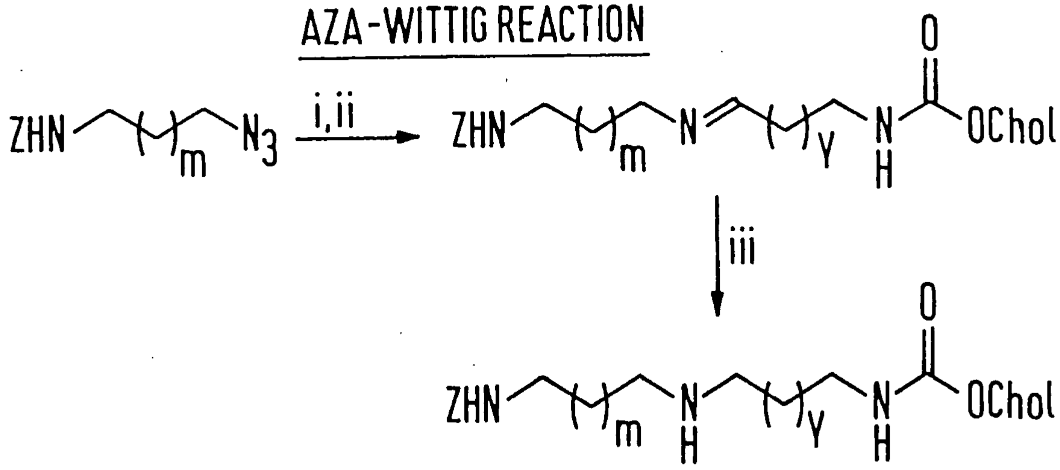
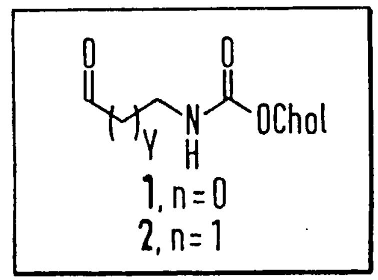


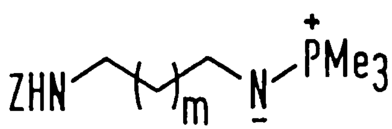
FIG. 14

AZA-WITTIG REACTION



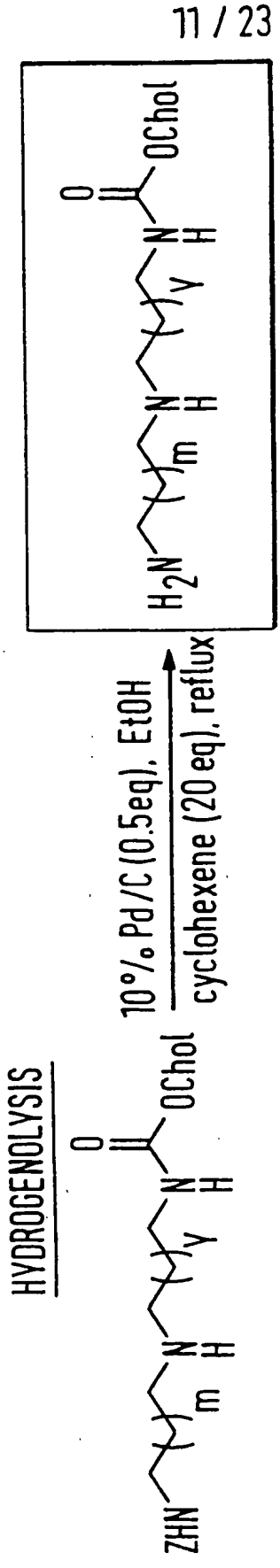


i) PMe_3 (1.1 eq), 4Å MS (1 g / mmol), THF, 0.75 hrs; ii) **1** or **2** (1.2 eq) in THF, 5-18 hrs;
iii) $NaBH_4$ / diglyme (2.0 eq), EtOH, 24 hrs

via 

m	Y	Yield (%)
0	0	79
1	0	72
2	0	89
0	1	83
1	1	87
2	1	90

FIG. 15



m	Y	Yield (%)
0	0	99
1	0	99
2	0	99
0	1	99
1	1	99
2	1	99

FIG. 16

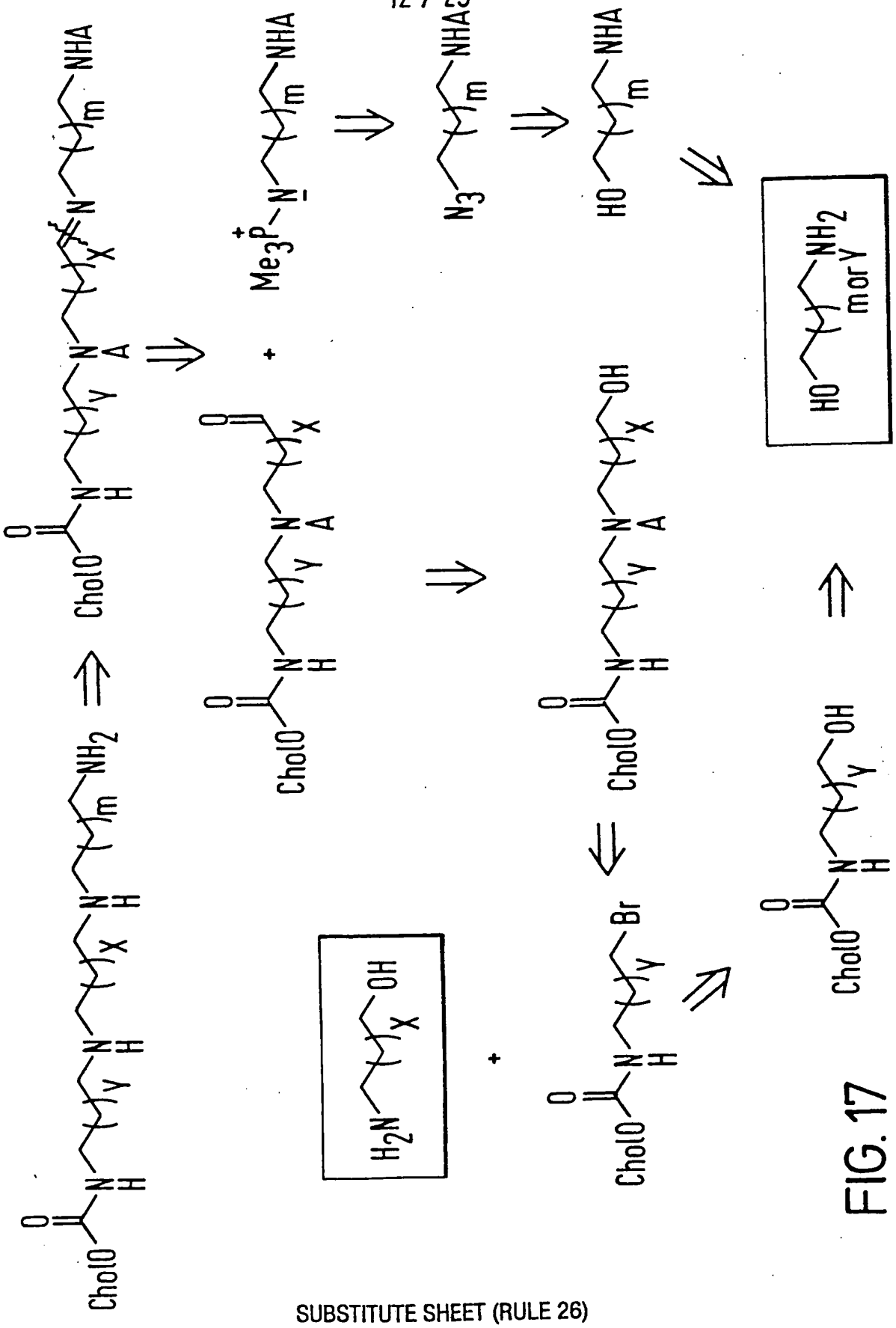
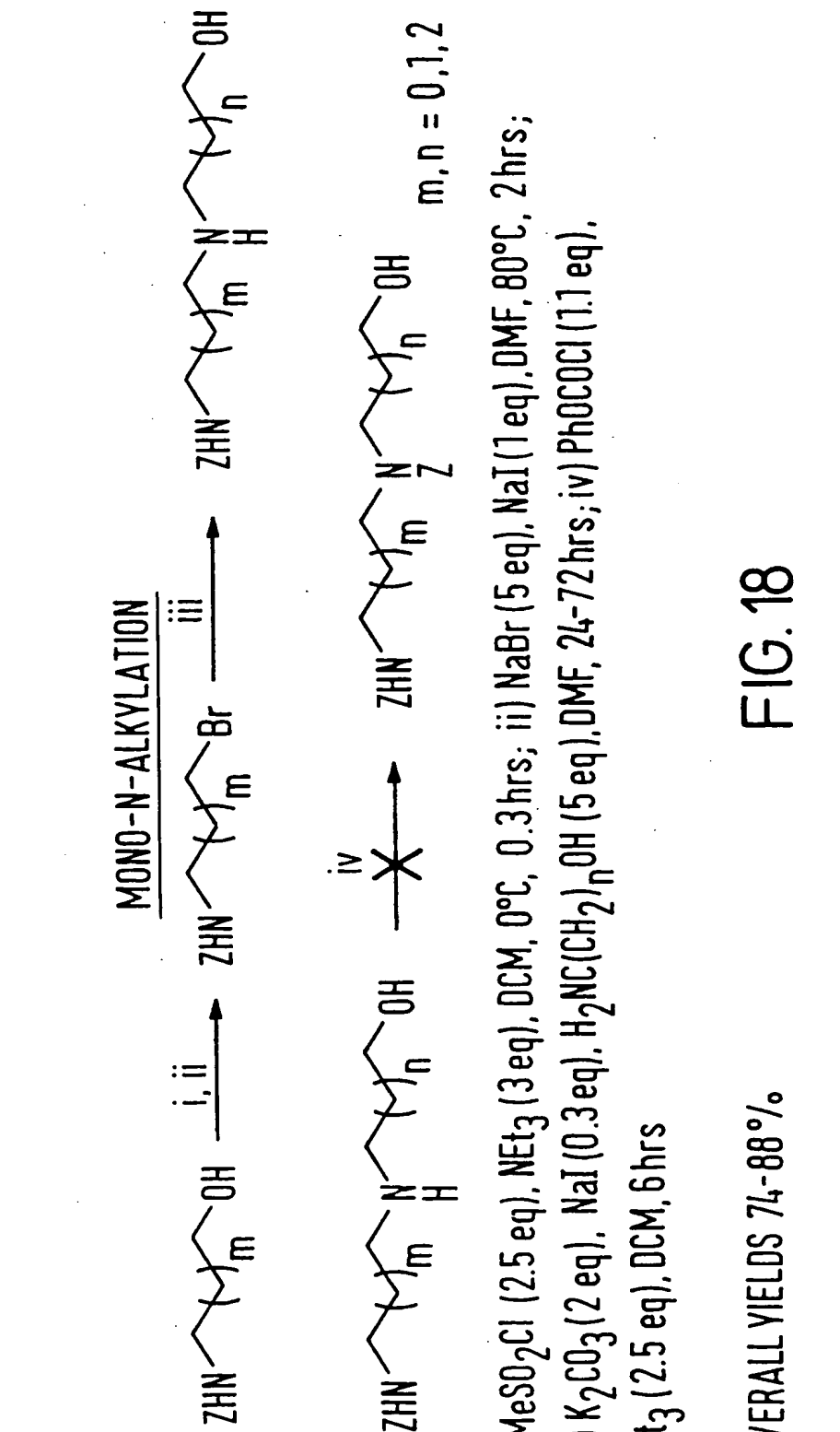


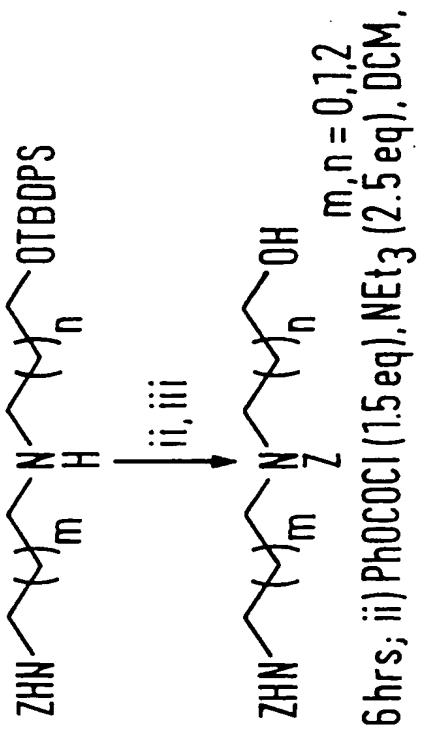
FIG. 17



i) $MeSO_2Cl$ (2.5 eq), NEt_3 (3 eq), DCM, 0°C, 0.3hrs; ii) NaBr (5 eq), NaI (1 eq), DMF, 80°C, 2hrs;
iii) K_2CO_3 (2 eq), NaI (0.3 eq), $H_2NC(CH_2)_nOH$ (5 eq), DMF, 24-72hrs; iv) PhOCOCl (1.1 eq), NEt_3 (2.5 eq), DCM, 6hrs

OVERALL YIELDS 74-88%

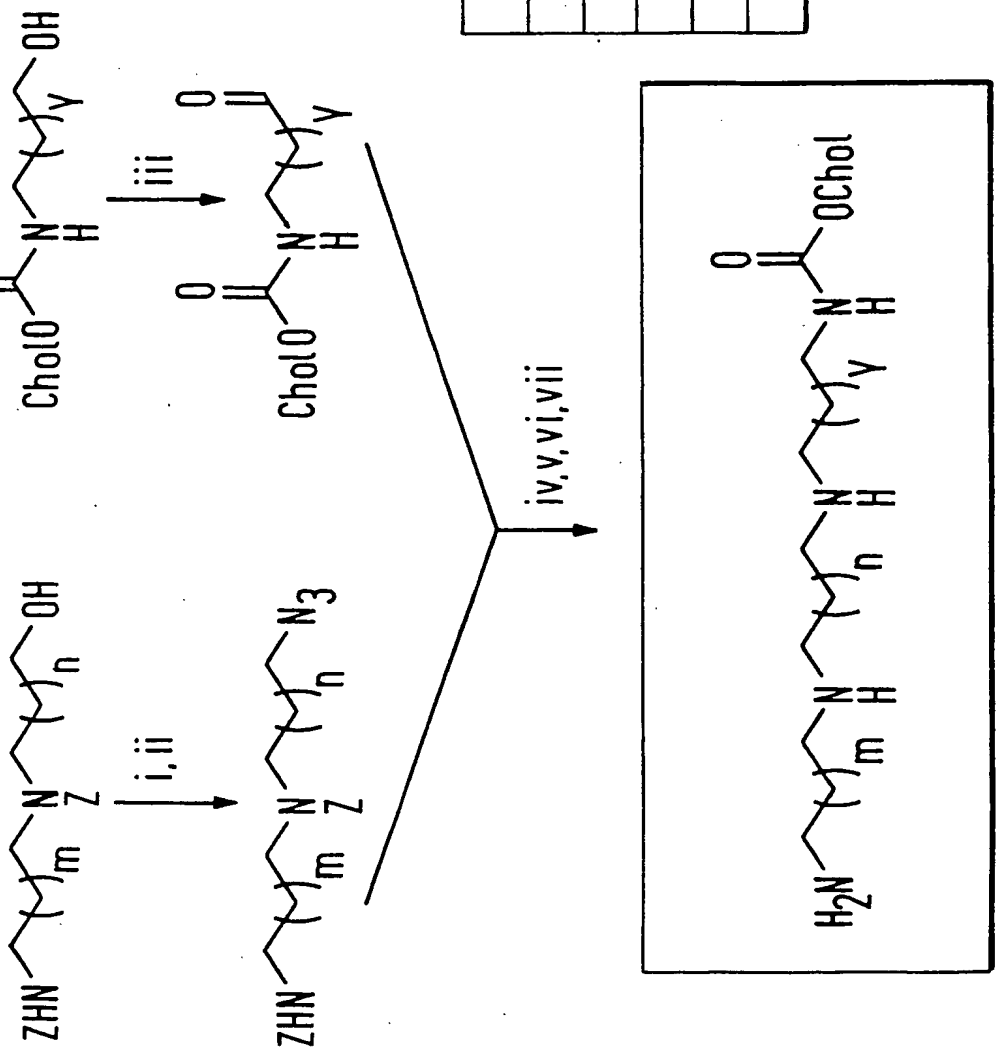
FIG. 18



i) TBDPS-Cl (1.5 eq), NEt_3 (3 eq), cat, DMAP, DCM, 4-6hrs; ii) PhOCOCl (1.5 eq), NEt_3 (2.5 eq), DCM, 6hrs; iii) TBAF (1 eq), THF, 1-2hrs
OVERALL YIELDS 60-82%

FIG. 19

APPLICATION TO SYNTHESIS OF SPERMINOLIPIDS

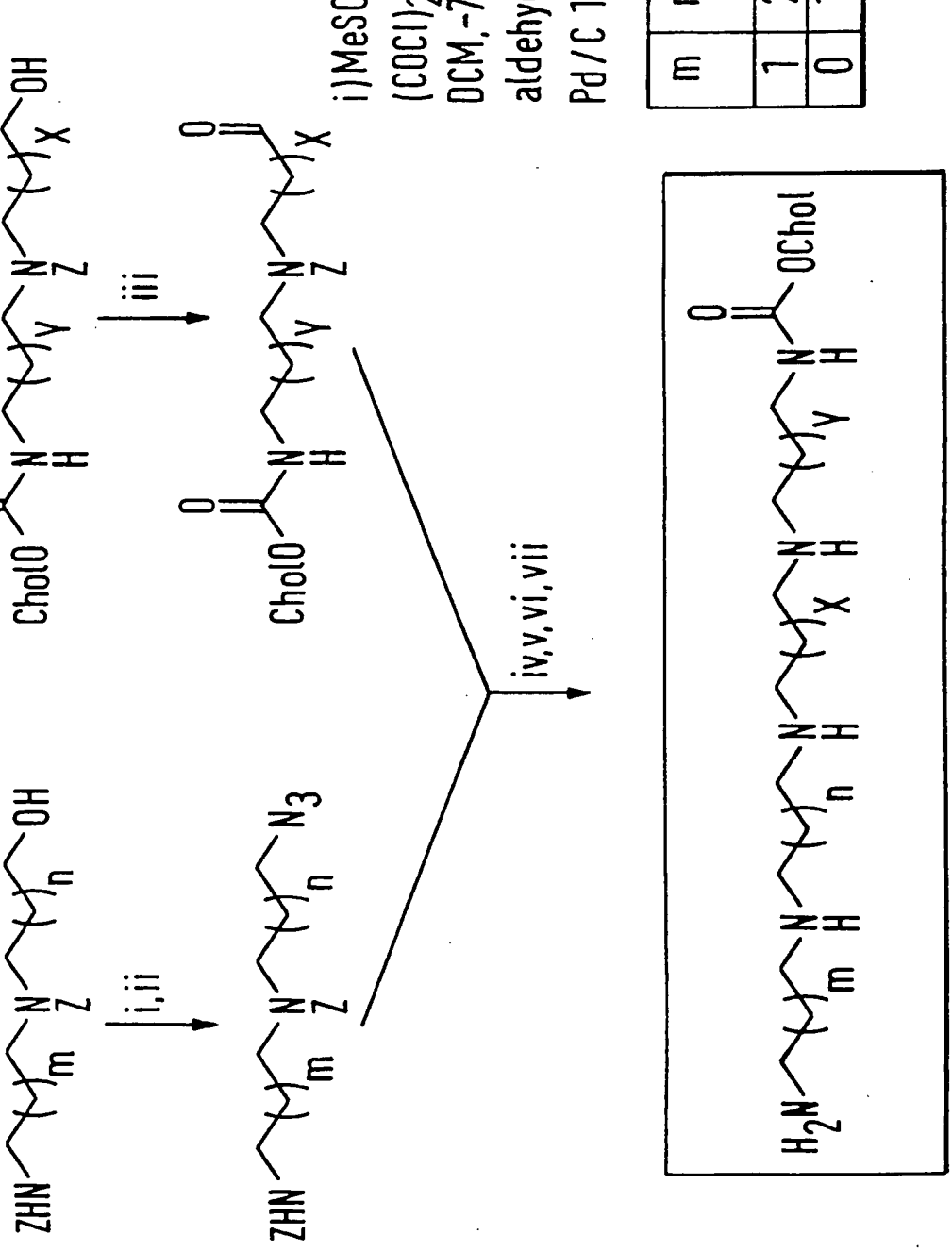


m	n	Y	Yield (%)
0	1	0	54
0	1	1	69
0	2	1	80
1	2	1	71
1	0	0	64

FIG. 20

FIG. 21

APPLICATION TO SYNTHESIS OF PENTAMINOLIPIDS



m	n	X	Y	Yield (%)
1	2	2	1	56
0	1	2	1	74

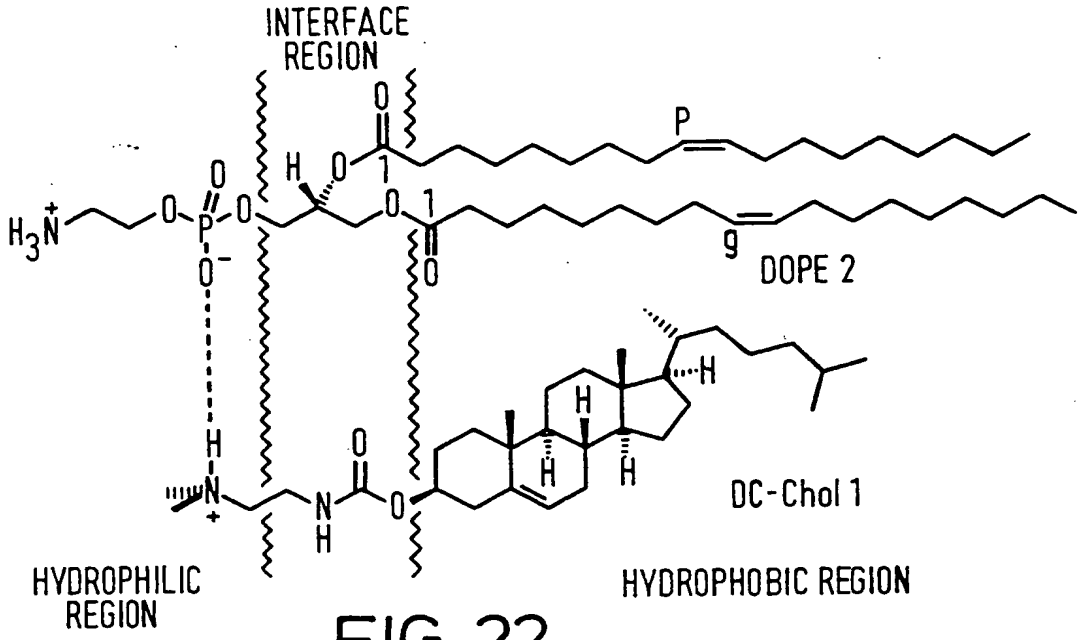

INTERFACE
REGION
DOPE 2
DC-Chol 1
HYDROPHILIC
REGION
HYDROPHOBIC REGION

FIG. 22

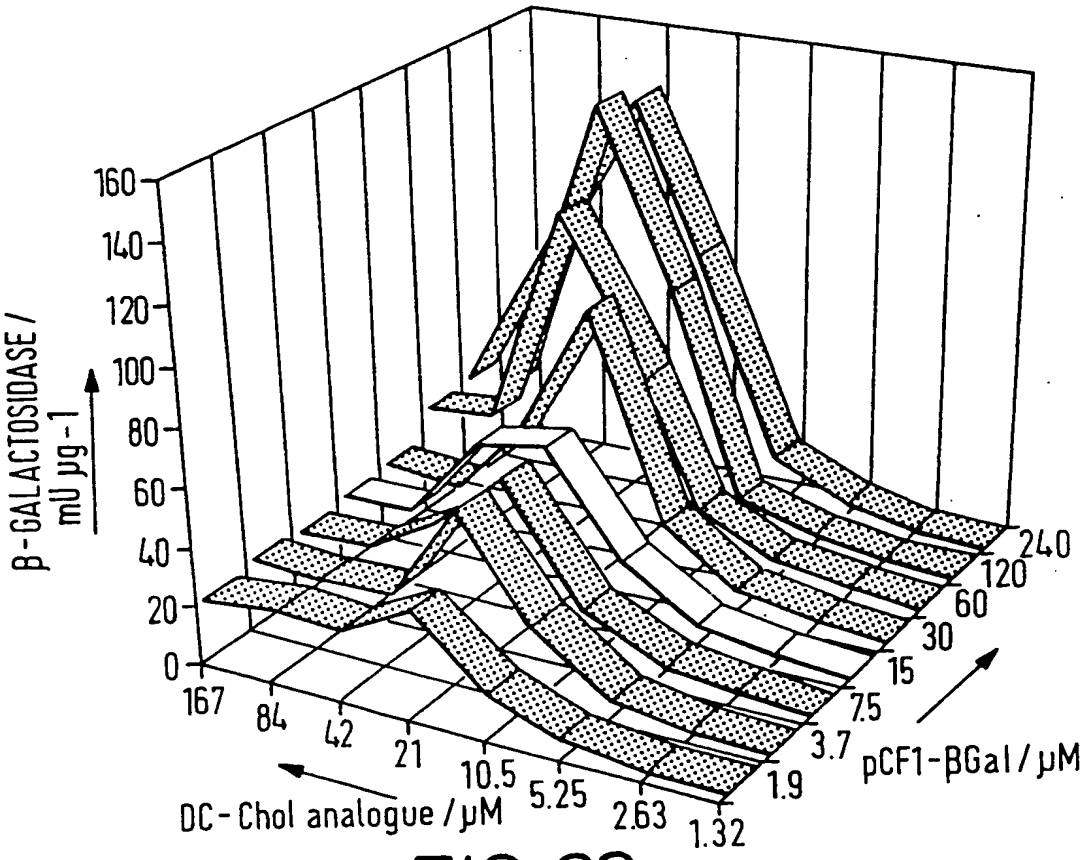

β-GALACTOSIDASE /
mU µg-1
160
140
120
100
80
60
40
20
0
167
84
42
21
10.5
5.25
2.63
1.32
DC-Chol analogue / µM
24.0
120
60
30
15
7.5
3.7
1.9
pCF1-βGal / µM

FIG. 23

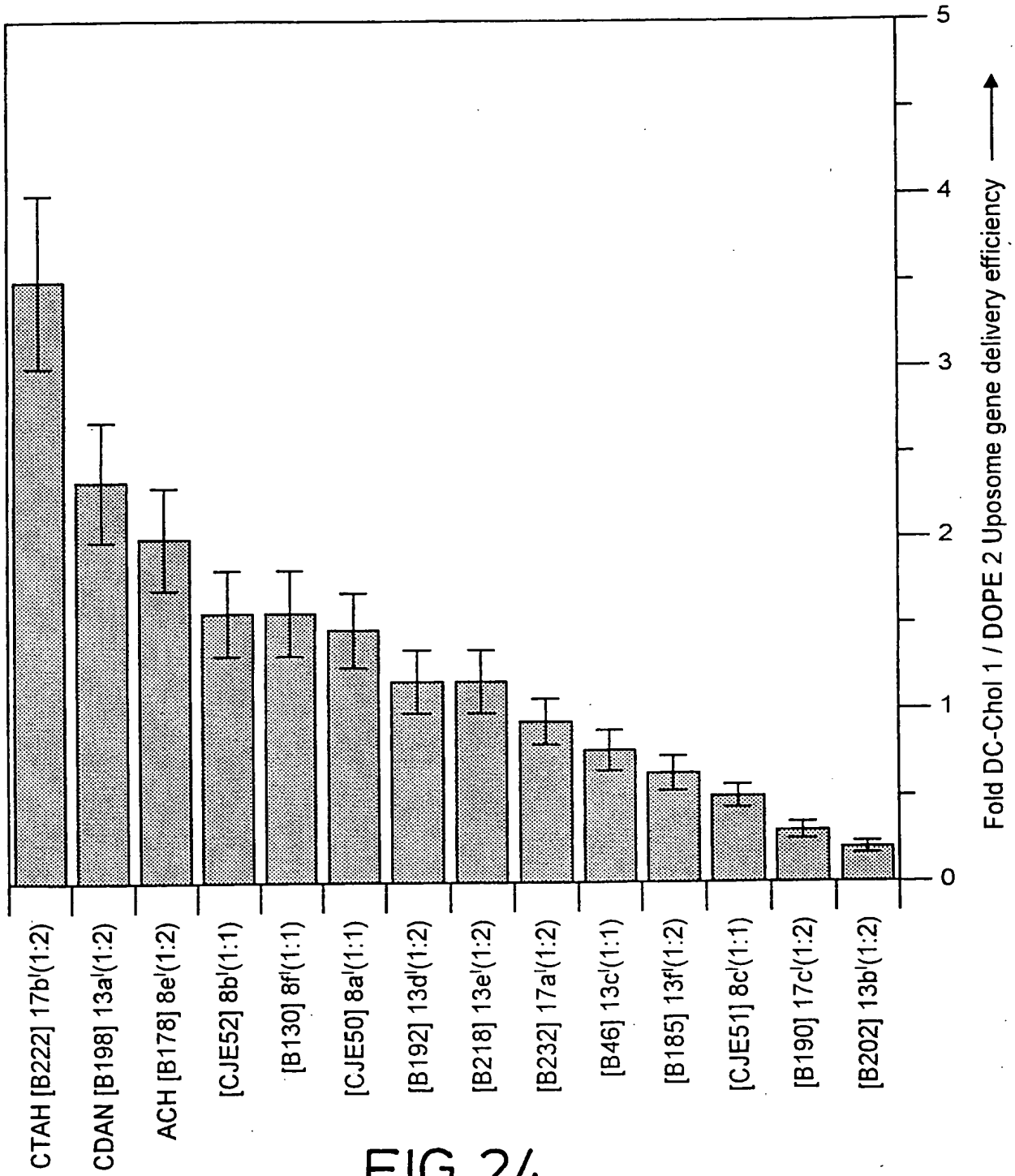

5
4
3
2
1
0
Fold DC-Chol 1 / DOPE 2 Uposome gene delivery efficiency
CTAH [B222] 17b'(1:2)
CDAN [B198] 13a'(1:2)
ACH [B178] 8e'(1:2)
[CJE52] 8b'(1:1)
[B130] 8f'(1:1)
[CJE50] 8a'(1:1)
[B192] 13d'(1:2)
[B218] 13e'(1:2)
[B232] 17a'(1:2)
[B46] 13c'(1:1)
[B185] 13f'(1:2)
[CJE51] 8c'(1:1)
[B190] 17c'(1:2)
[B202] 13b'(1:2)

FIG. 24

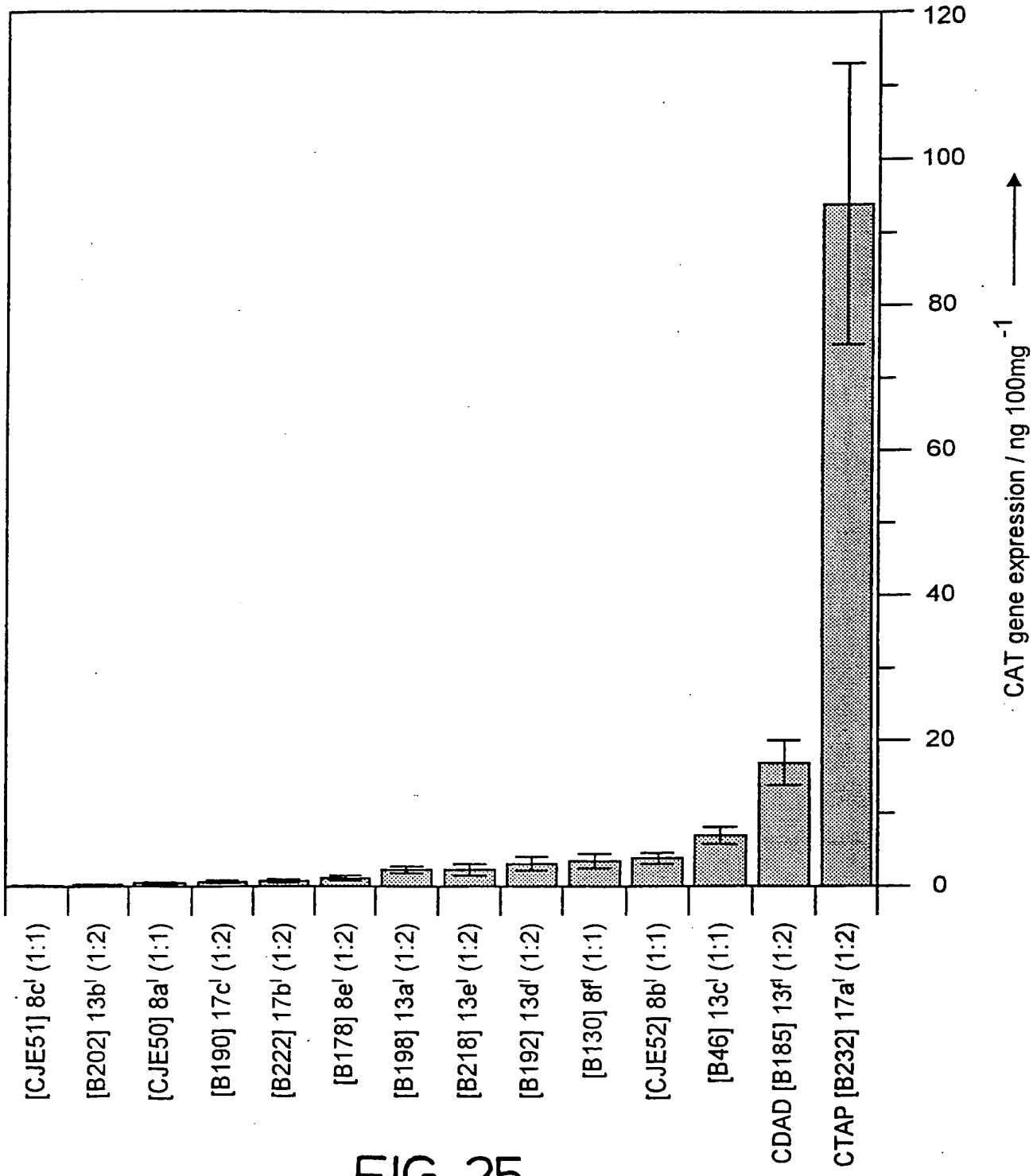

120
100
80
60
40
20
0
CAT gene expression / ng 100mg -1
[CJE51] 8c' (1:1)
[B202] 13b' (1:2)
[CJE50] 8a' (1:1)
[B190] 17c' (1:2)
[B222] 17b' (1:2)
[B178] 8e' (1:2)
[B198] 13a' (1:2)
[B218] 13e' (1:2)
[B192] 13d' (1:2)
[B130] 8f' (1:1)
[CJE52] 8b' (1:1)
[B46] 13c' (1:1)
CDAD [B185] 13f' (1:2)
CTAP [B232] 17a' (1:2)

FIG. 25

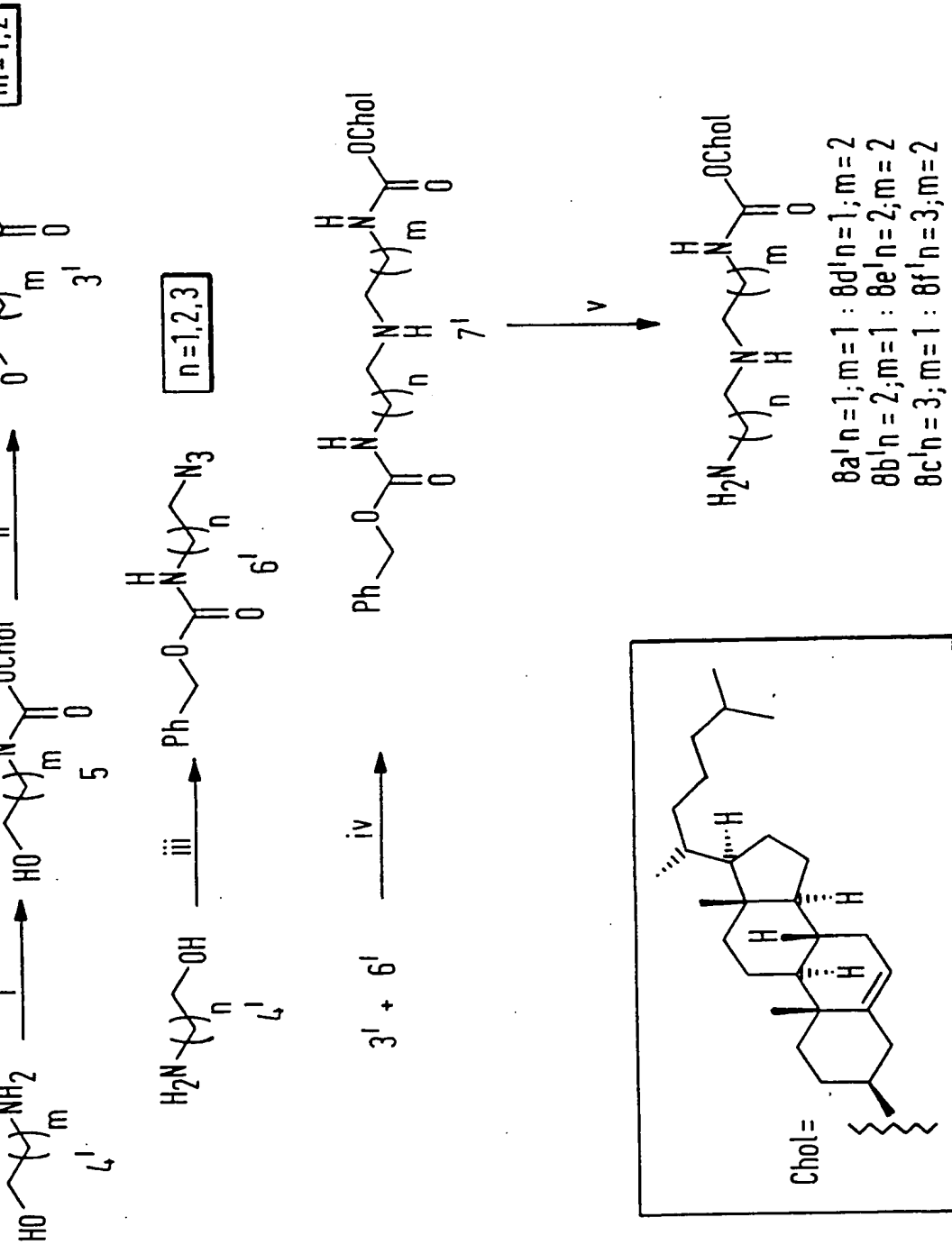
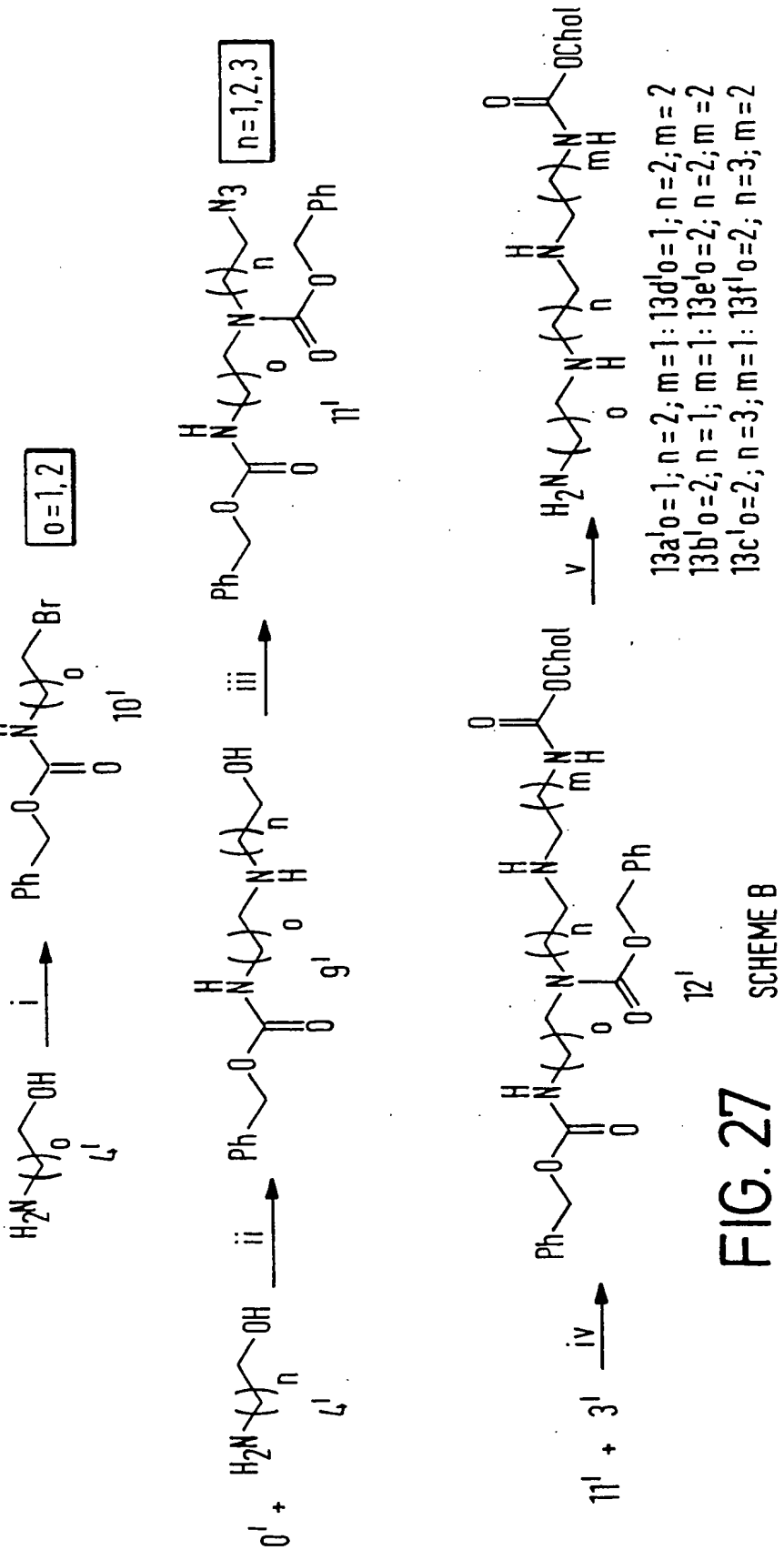

m=1,2
n=1,2,3
i
ii
iii
iv
v
OChol
Chol=
8a' n=1; m=1 : 8d' n=1; m=2
8b' n=2; m=1 : 8e' n=2; m=2
8c' n=3; m=1 : 8f' n=3; m=2
SCHEME A

FIG. 26



$13a^1$ o=1; n=2; m=1: $13d^1$ o=1; n=2; m=2
$13b^1$ o=2; n=1; m=1: $13e^1$ o=2; n=2; m=2
$13c^1$ o=2; n=3; m=1: $13f^1$ o=2; n=3; m=2

FIG. 27

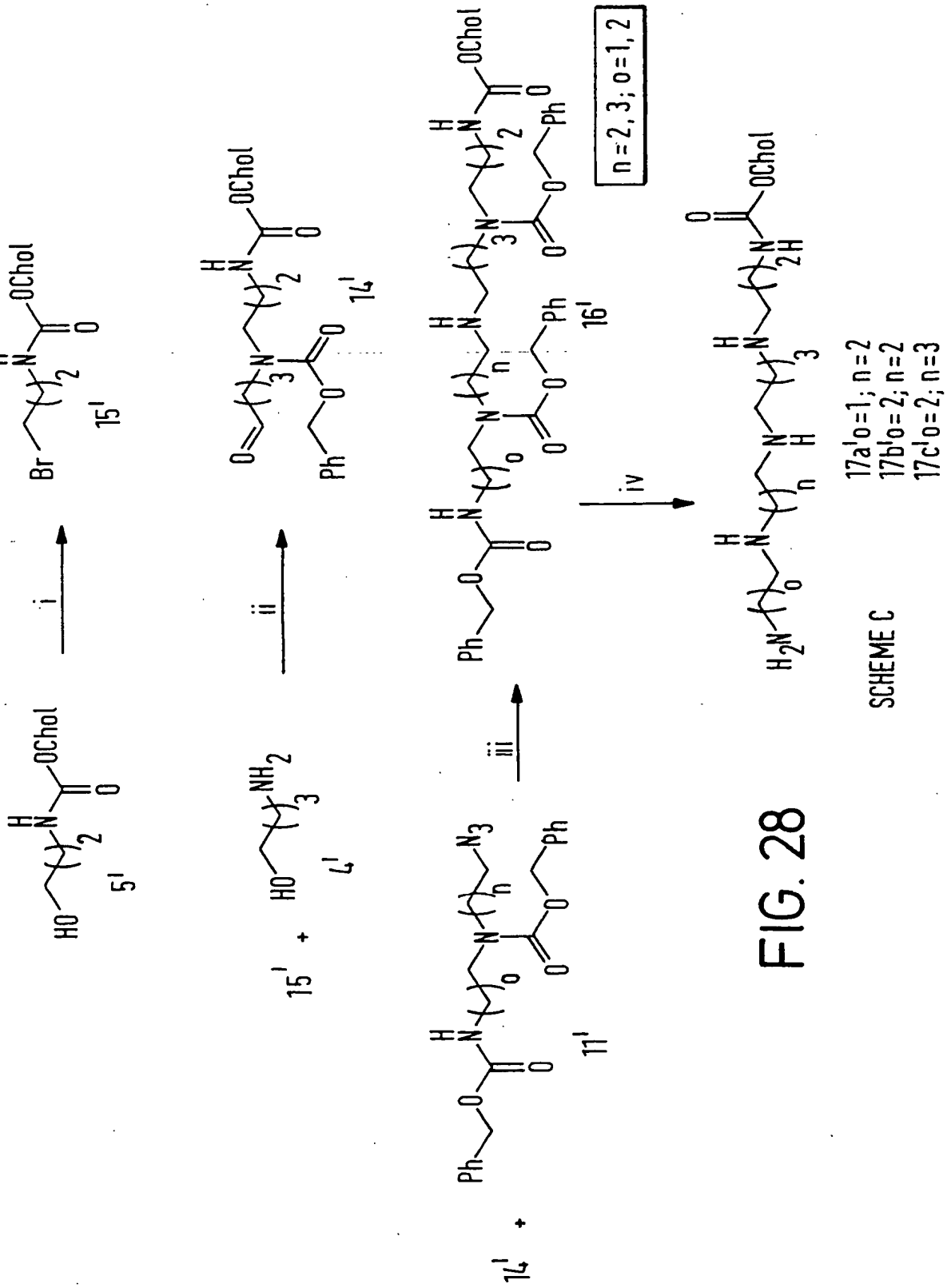
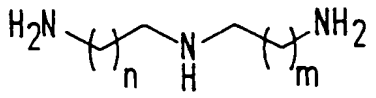
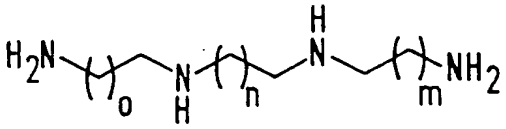


FIG. 28

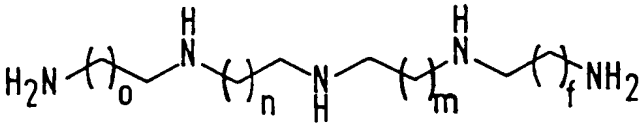
SCHEME C



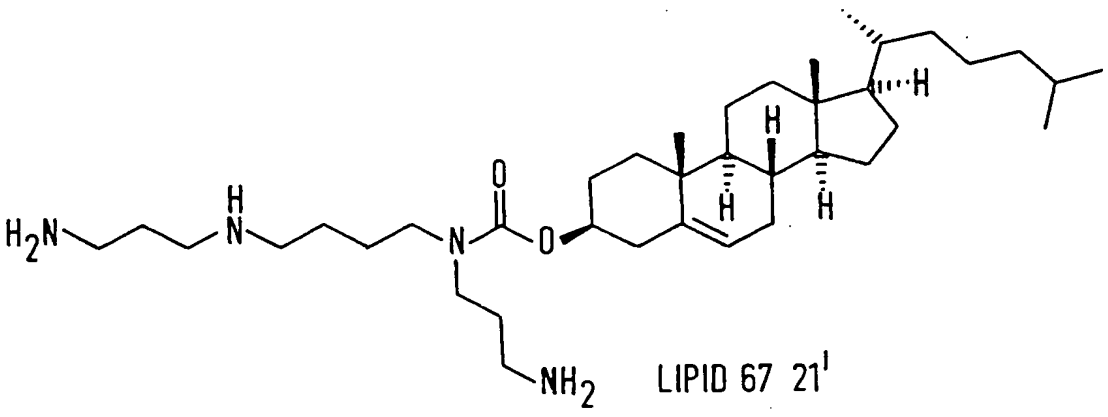
18' n = 3; m = 2



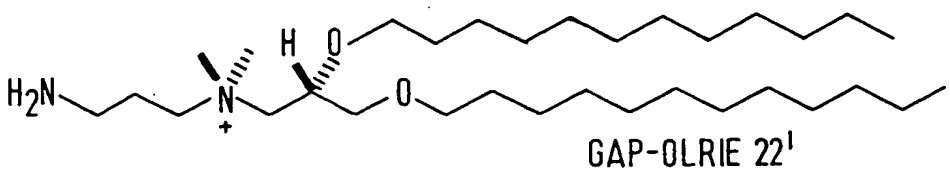
19' o = 2; n = 3; m = 2



20' f, m, n, o = 2



LIPID 67 21'



GAP-OLRIE 22'

FIG. 29